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# (U) Nerve Agent

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**Nerve Agents** (also known as **nerve gases**, though these chemicals are liquid at room temperature) are a class of phosphorus-containing organic chemicals (organophosphates) that disrupt the mechanism by which nerves transfer messages to organs. The disruption is caused by blocking acetylcholinesterase, an enzyme that normally relaxes the activity of acetylcholine, a neurotransmitter.

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## Overview

As chemical weapons, they are classified as weapons of mass destruction by the United Nations according to UN Resolution 687, and their production and stockpiling was outlawed by the Chemical Weapons Convention of 1993; the Chemical Weapons Convention officially took effect on April 29 1997.

Poisoning by a nerve agent leads to contraction of pupils, profuse salivation, convulsions, involuntary urination and defecation, and eventual death by asphyxiation as control is lost over respiratory muscles. Some nerve agents are readily vaporized or aerosolized and the primary portal of entry into the body is the respiratory system. Nerve agents can also be absorbed through the skin, requiring that those likely to be subjected to such agents wear a full body suit in addition to a respirator.

## Biological Effects

As their name suggests, nerve agents attack the nervous system of the human body. All such agents

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function the same way: by interrupting the breakdown of the neurotransmitters that signal muscles to contract, preventing them from relaxing.

Initial symptoms following exposure to sarin (and other nerve agents) are a runny nose, tightness in the chest and constriction of the pupils. Soon after, the victim will then have difficulty breathing, and will experience nausea and drooling. As the victim continues to lose control of his or her bodily functions, he or she will involuntarily salivate, lacrimate, urinate, defecate, experience gastrointestinal pain, and emesis (vomiting). This phase is followed by twitching and jerking, and ultimately the victim will become comatose and suffocate as a consequence of convulsive spasms.

The effects of nerve agents are very long lasting and cumulative (increased successive exposures), and survivors of nerve agent poisoning almost invariably suffer chronic neurological damage.

## Mechanism of Action

When a normally functioning motor nerve is stimulated it releases the neurotransmitter acetylcholine, which transmits the impulse to a muscle or organ. Once the impulse is sent, the enzyme acetylcholine esterase immediately breaks down the acetylcholine in order to allow the muscle or organ to relax.

Nerve agents disrupt the nervous system by inhibiting the enzyme acetylcholine esterase by forming a covalent bond with the site of the enzyme where acetylcholine normally undergoes hydrolysis (breaks down). The result is that acetylcholine builds up and continues to act so that any nerve impulses are continually transmitted, and muscle contractions do not stop.

This same action also occurs at the gland and organ levels, resulting in uncontrolled drooling, tearing of the eyes (lacrimation), and excess production of mucous from the nose (rhinorrhea).

## Antidotes

Atropine and related anticholinergic drugs (some synthetic anticholinergics, such as biperiden may counteract the central symptoms of nerve agent poisoning better than atropine, since they pass the blood-brain barrier better than atropine) act as antidotes to nerve agent poisoning because they block acetylcholine receptors, but they are poisonous in their own right. While they will save the life of a person affected with nerve agents, that person may be incapacitated briefly or for an extended period of time, depending on the amount of exposure. The endpoint of atropine administration is the clearing of bronchial secretions. Atropine for field use by military personnel is often loaded in an autoinjector, for ease of use in stressful conditions.

Pralidoxime chloride, also known as *2-PAM chloride*, is also used as an antidote. Rather than counteracting the initial effects of the nerve agent on the nervous system like atropine, *pralidoxime chloride* actually re-activates the poisoned enzyme (acetylcholinesterase) by "scavenging" the phosphoryl rest attached on the functional hydroxyl group of the enzyme. Though safer to use, it takes a longer time to have an effect.

Recent scientific breakthroughs have seen antidotes being produced in the milk of genetically modified goats.<sup>[1]</sup>

## Classes

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There are two main classes of nerve agents. The members of the two classes share similar properties, and are given both a common name (such as *sarin*), and a two-character NATO identifier (such as GB).

## G-Series

*"G" redirects here; for other uses, see G (disambiguation).*

The *G-series* is thus named because German scientists first synthesized them. All of the compounds in this class were discovered and synthesized during or soon after World War II, led by Dr. Gerhard Schrader (later under the employment of I.G. Farben).

This series is the first and oldest family of nerve agents. The first nerve agent ever synthesised was GA (tabun) in 1936. GB (sarin) was discovered next in 1938, followed by GD (soman) in 1944 and finally the more obscure GF (cyclosarin) in 1949. GB was the only G agent that was fielded by the USA as a munition, specifically in rockets, aerial bombs, howitzer rounds, and gun rounds.<sup>[2]</sup>

## V-Series

The *V-series* is the second family of nerve agents (the *V* apparently standing for "venomous"), and also contains four members: VE, VG, VM, and VX. The most studied agent in this family, VX, was invented in the 1950s at Porton Down in the United Kingdom. The other agents in this series have not been studied extensively, and information about them is limited. It is known, however, that the V-series agents are about 10 times more toxic than the G-agent sarin (GB).

All of the V-agents are *persistent agents*, meaning that these agents do not degrade or wash away easily, and can therefore remain on clothes and other surfaces for long periods. In use, this allows the V-agents to be used to blanket terrain to guide or curtail the movement of enemy ground forces. The consistency of these agents is similar to oil; as a result, the contact hazard for V-agents is primarily - but not exclusively - dermal. VX was the only V-series agent that was fielded by the USA as a munition, consisting of rockets, artillery shells, and landmines<sup>[2]</sup>

## Novichok Agents

The Novichok (Russian for "newcomer") agents are a recently developed series of organophosphate compounds developed in the Soviet Union. The advantage to using new agents is that they have never been previously encountered. As a result:

- potentially, no specific treaties banning their possession or use exist
- existing detection and warning devices cannot detect these agents on the battlefield
- existing protective equipment (eg gasmasks) will not protect troops from being poisoned

## Insecticides

A number of insecticides, the phenothiazines, organophosphates such as dichlorvos, malathion and parathion, are nerve agents. The metabolism of insects is sufficiently different from mammals that these compounds have little effect on humans and other mammals at proper doses; but there is considerable concern about the effects of long-term exposure to these chemicals by farm workers and animals alike.

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At high enough doses, however, acute toxicity and death can occur through the same mechanism as other nerve agents. Organophosphate pesticide poisoning is a major cause of disability in many developing countries, and is often the preferred method of suicide.<sup>[3]</sup>

Lately, concern has also been expressed that commercial pilots, flight attendants, and frequent fliers are being poisoned by the organophosphate jet engine oil leaking into the aircraft air conditioning system.<sup>[4]</sup>

## History

### The Discovery of Nerve Agents

This first class of nerve agents, the so-called *G-Series*, was accidentally discovered in Germany on 23 December 1936 by a research team headed by Dr. Gerhard Schrader. Since 1934, Schrader had been in charge of a laboratory in Leverkusen to develop new types of insecticides for IG Farben. While working toward his goal of improved insecticide, Schrader experimented with numerous fluorine-containing compounds, eventually leading to the preparation of tabun.

In experiments, tabun was extremely potent against insects: as little as 5 ppm of tabun killed all the leaf lice he used in his initial experiment. In January 1937, Schrader observed the effects of nerve agents on human beings first-hand when a drop of tabun spilled onto a lab bench. Within minutes he and his laboratory assistant began to experience miosis (constriction of the pupils of the eyes), dizziness, and severe shortness of breath. It took them three weeks to recover fully.

In 1935 the Nazi leadership had passed a decree that required all inventions of possible military significance to be reported to the Ministry of War, so in May of 1937 Schrader sent a sample of tabun to the chemical warfare (CW) section of the Army Weapons Office in Berlin-Spandau. Dr. Schrader was summoned to the Wehrmacht chemical lab in Berlin to give a demonstration, after which Schrader's patent application and all related research was classified. Colonel Rüdiger, head of the CW section, ordered the construction of new laboratories for the further investigation of tabun and other organophosphate compounds, and Schrader soon moved to a new laboratory at Wuppertal-Elberfeld in the Ruhr valley to continue his research in secret throughout World War II.

Three of the most widely known agents, sarin (GB), soman (GD), and tabun (GA) were also developed during this period for use as chemical warfare agents, but were not used in combat. Cyclosarin (GF) was developed somewhat later, in 1949, by the same team. The prefix "G" was used in the names of all the chemicals because they were of German origin<sup>[5]</sup>.

### The Nazi Mass Production of Tabun

In 1939, a pilot plant for tabun production was set up at Munster-Lager, on Luneberg heath near the German Army proving grounds at Raubkammer. In January 1940, construction began on a secret plant, code named "Hochwerk" (*High factory*), for the production of tabun at Dyhernfurth an der Oder (now Brzeg Dolny in Poland), on the Oder River 40 km (24.9 miles) from Breslau (now Wrocław) in Silesia.

The plant was large, covering an area of 2.4 by 0.8 km (1.5 by 0.5 miles), and was completely self-contained, synthesizing all intermediates as well as the final product, tabun. The factory even had an underground plant for filling munitions, which were then stored at Krappitz (now Krapowice) in Upper

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Silesia. The plant was operated by Anorgana GmbH, a subsidiary of IG Farben, as were all other chemical weapon agent production plants in Germany at the time.

Because of the plant's deep secrecy and the difficult nature of the production process, it took from January 1940 until June 1942 for the plant to become fully operational. Many of tabun's chemical precursors were so corrosive that reaction chambers not lined with quartz or silver soon became useless. Tabun itself was so hazardous that the final processes had to be performed while enclosed in double glass-lined chambers with a stream of pressurized air circulating between the walls.

3,000 German nationals were employed at Hochwerk, all equipped with respirators and clothing constructed of a poly-layered rubber/cloth/rubber sandwich that was destroyed after the tenth wearing. Despite all precautions, there were over 300 accidents before production even began, and at least 10 workers died during the 2.5 years of operation. Some incidents cited in *A Higher Form of Killing: The Secret History of Chemical and Biological Warfare* are as follows:

- Four pipe fitters had liquid tabun drain onto them; they died before their rubber suits could be removed.
- A worker had 2 liters of tabun pour down the neck of his rubber suit; he died within 2 minutes.
- Seven workers were hit in the face with a stream of tabun of such force that the liquid was forced behind their respirators; only two survived despite heroic resuscitation measures.

The plant produced between 10,000 and 30,000 tons of tabun before its capture by the Soviet Army.<sup>[5]</sup>

### Nerve Agents in Nazi Germany

In mid-1939, sarin was invented, and the formula for the agent was passed to the Chemical Warfare section of the German Army Weapons Office, which ordered that it be brought into mass production for wartime use. A number of pilot plants were built, and a high-production facility was under construction (but was not finished) by the end of World War II. Estimates for total sarin production by Nazi Germany range from 500 kg to 10 tons.

During that time, German intelligence believed that the Allies also knew of these compounds, assuming that because these compounds were not discussed in the Allies' scientific journals information about them was being suppressed. Though sarin, tabun and soman were incorporated into artillery shells, the German government ultimately decided not to use nerve agents against Allied targets. The Allies didn't learn of these agents until shells filled with them were captured towards the end of the war.

This is detailed in Joseph Borkin's book *The Crime and Punishment of IG Farben*:

Speer, who was strongly opposed to the introduction of tabun, flew Otto Ambros, I.G.'s authority on poison gas as well as synthetic rubber, to the meeting. Hitler asked Ambros, "What is the other side doing about poison gas?" Ambros explained that the enemy, because of its greater access to ethylene, probably had a greater capacity to produce mustard gas than Germany did. Hitler interrupted to explain that he was not referring to traditional poison gases: "I understand that the countries with petroleum are in a position to make more [mustard gas], but Germany has a special gas, tabun. In this we have a monopoly in Germany." He specifically wanted to know whether the enemy had access to such a gas and what it was doing in this area. To Hitler's disappointment Ambros replied, "I have justified reasons to assume that tabun, too, is known abroad. I know that tabun was publicized as

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early as 1902, that Sarin was patented, and that these substances appeared in patents. (...) Ambros was informing Hitler of an extraordinary fact about one of Germany's most secret weapons. The essential nature of tabun and sarin had already been disclosed in the technical journals as far back as 1902, and I.G. had patented both products in 1937 and 1938. Ambros then warned Hitler that if Germany used tabun, it must face the possibility that the Allies could produce this gas in much larger quantities. Upon receiving this discouraging report, Hitler abruptly left the meeting. The nerve gases would not be used, for the time being at least, although they would continue to be produced and tested.<sup>[6]</sup>

## The Secret Gets Out

After World War II, the Allies recovered German artillery shells containing the three German nerve agents of the day, prompting further research into nerve agents by the former Allies. In 1952, researchers in Porton Down, England invented the VX nerve agent, but soon abandoned the project. In 1958 the British government traded their VX technology with the United States of America in exchange for information on thermonuclear weapons; by 1961 the US was producing large amounts of VX, and performed its own nerve agent research. This research produced three more agents; the four agents (VE, VG, VM, VX) are collectively known as the "V-Series" class of nerve agents.

## Since World War II

To date, the only large scale use of chemical weapons, including nerve agents, was Iraq's chemical war against Iran (Iran-Iraq war of 1981-1988); the Kurdish village of Halabja was exposed to chemical weapons, reportedly including tabun. Nerve agents were not used by Iraq in the Gulf War, though a number of U.S. and UK personnel were exposed to them when the Khamisiyah chemical depot was destroyed. This and the widespread use of anticholinergic drugs as a protective treatment against nerve gas attack has been proposed as a possible cause of Gulf war syndrome.

One of the most widely publicised uses of nerve agents was the 1995 terrorist attack in which operatives of the group Aum Shinrikyo released sarin into the Tokyo subway system.

## Ocean Disposal of Chemical Weapons

In 1972, The United States Congress banned the practice of disposing chemical weapons into the ocean. However 32,000 tons of nerve and mustard agents had already been dumped into the ocean waters off of the United States by the U.S. Army. According to a 1998 report created by William Brankowitz, a deputy project manager in the U.S. Army Chemical Materials Agency, the Army created at least 26 chemical weapons dumpsites in the ocean off of at least 11 states on both the west and east coasts. Additionally due to poor records, currently they only know the rough whereabouts of half of them.

It is unknown how these dumps of chemical weapons have affected the ocean ecology—it may be responsible for some of the decline in fish populations over the past decades, but no evidence has yet proved a causal relationship between dumping and fish population decline. The steel containers they are contained within face a variable rate of decay and no one is really certain where or how deep they were dumped. If a nerve agent leaks into the ocean, it can last up to six weeks, during which time it will kill every susceptible organism it touches before it breaks down into its nonlethal chemical components.

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## Popular Culture

As a weapon of fear and terror, nerve agents are quickly becoming a staple in the plots of television, cinema, and video games. In most implementations of this plot, a shadowy terrorist organization obtains a quantity of nerve agent and threatens to release it in a population center.

A fictional nerve agent, ZV, is an integral part of the story line for John Lange's (a pseudonym of Michael Crichton) 1972 novel *Binary*. The effects of this agent were the same as the V-series agents and the book mentions these other agents although it does not mention other existing binary nerve agents such as the G-series or VX.

In *Mobile Suit Zeta Gundam*, a fictional nerve agent called G3 is used against space colonists by the Earth Federation's Titans organization, setting off a chain of events culminating in the destruction of said group.

Nerve agents are among the armaments of the future Colonial Marines in the 1986 film *Aliens*, in which the character Vasquez suggests the use of fictional "CN-20" against an alien hive.

In the 1996 action movie, *The Rock*, a retired US Marine Brigadier General blackmails the government by threatening to attack San Francisco with rockets armed with VX gas. The film contained numerous inaccuracies, not the least of which including the description (and visual effects) of how VX affects a person: "your muscles freeze, you can't breathe, you spasm so hard you break your own back, spit your guts out--but that's after your skin melts off." Unlike the movie, atropine carried by actual U.S. military personnel is in the form of a sprung "auto-injector" which is applied to the thigh (not a long needle jabbed into the heart), and it is always followed by another injector containing 2-PAM Chloride. Also, and perhaps more glaringly erroneous (though theatrically horrific), VX does not melt skin.

In the 2002 movie *XXX*, a terrorist group called Anarchy-99 produces a fictitious binary nerve agent called "Silent Night," which decomposed and became harmless when passed through water.

In the movie *Saw II*, sarin is the nerve agent that the Jigsaw Killer uses as part of his game. However, his brief description of sarin's effects is inaccurate, as is much of the film's representation of how it works: it is highly improbable that the characters exposed to the gas would remain unaffected as long as they did. In addition, as sarin is an irreversible anticholinesterase inhibitor, its effects are permanent; no antidote, even if it were to exist, would be effective unless administered immediately following exposure.

This plot device was adopted by video game designers as well. For example, *Tom Clancy's Rainbow Six 3: Raven Shield* featured terrorists that attempted to poison the food supply with VX nerve agent. Also, it was the new deadly threat in *Syphon Filter: Dark Mirror*, where the nerve gas, Project Dark Mirror, was said to blend with oxygen, making it more lethal.

Before long, nerve agents began to appear on television. For example, VX was featured in the British television series *Spooks* as part of a simulated attack on the center of London, and recently, on season 5 of the primetime FOX series, *24*, Russian separatists manage to use a fictional, vaporised variant of VX called "Sentox VX-1" on several targets in Los Angeles.

The *Doctor Who* story *The Mind of Evil* involves the hijacking of a nerve gas missile destined to be destroyed, and in the later story *Terror of the Zygons* a Scottish village is drugged with a nerve gas

agent. Sarin was also featured in a later series of Spooks.

Author Greg Iles uses nerve agents sarin and soman in the plot for his World War II thriller *Black Cross*.

The South African post-grunge band Seether was first known as "Saron Gas".

The Canadian industrial band Skinny Puppy wrote a song called "VX Gas Attack" (from the album *VIVISectVI*) which deals lyrically with the Iraqi VX bomb attack on Iran in 1988.

In the Gulf War biography *Jarhead*, the protagonist, Anthony Swofford, is given an atropine autoinjector to counter VX gas.

In the horror sci-fi film *28 Weeks Later* Doyle has to cover his face to stop himself breathing in nerve gas while trying to jump start a car.

In the book *World War Z*, the Russian government drops VX Gas on hordes of refugees to reveal any carrying the zombie virus.

In the Steven Spielberg film *Close Encounters of the Third Kind* nerve gas is used as an excuse for the evacuation of the UFO landing site.

In the episode I Spy Apocalypse of the second series of spooks an EERIE exercise uses the gas as a test to evaluate the performance of the team under pressure. The gas is never released but the team are sealed on the grid and so believe that it has wiped out London .

## References and External Links

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| Blood Agents                                              |                          |                  |                    | Blister Agents        |                                   |                                   |          |
| Cyanogen Chloride<br>(CK)                                 | Hydrogen Cyanide<br>(AC) | Cyanide          |                    | Lewisite<br>(L)       | Sulfur Mustard<br>(HD/H/HT/HL/HQ) | Nitrogen Mustard<br>(HN1/HN2/HN3) |          |
| Nerve Agents                                              |                          |                  |                    |                       |                                   |                                   |          |
| G-Agents:                                                 |                          |                  |                    | V-Agents:             |                                   |                                   |          |
| Tabun<br>(GA)                                             | Sarin<br>(GB)            | Soman<br>(GD)    | Cyclosarin<br>(GF) | GV                    | VE                                | VG                                | VM<br>VX |
| Novichok Agents                                           |                          |                  |                    |                       |                                   |                                   |          |
| Pulmonary Agents                                          |                          |                  |                    | Incapacitating Agents |                                   |                                   |          |
| Chlorine                                                  | Chloropicrin<br>(PS)     | Phosgene<br>(CG) | Diphosgene<br>(DP) | Agent 15<br>(BZ)      | Kolokol-1                         |                                   |          |
| Riot Control Agents                                       |                          |                  |                    |                       |                                   |                                   |          |
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